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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,628	12/01/2000	Katherine Armstrong	50,597	4194

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	9

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/727,628	ARMSTRONG ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1 April 2003 has been entered.

2. Claims 6 and 9-16 have been cancelled and claims 17-26 have been added, as requested in Paper No. 8, filed 1 April 2003. Claims 17-26 are pending.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

4. Claims 17 and 24 are objected to because of the following informalities:

In claim 17, line 2, and claim 24, line 4, --wherein-- should be inserted after the comma.

There is an improper article before "nucleic" in claim 17, line 2.

Claim Rejections - 35 USC § 112

5. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "fragments of SEQ ID NO:3 containing at least about 23 contiguous nucleotides of

7-2064 of SEQ ID NO:3". Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

6. Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promoter of bases 7-2064 of SEQ ID NO:3, does not reasonably provide enablement for nucleic acids that comprise fragments of at least 23 or 200 bases or variants with 95% homology to bases 7-2064 of SEQ ID NO:3 or the fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 6 December 2002, as applied to claims 9-12 and 14-16. Applicant's arguments filed 1 April 2003 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of nucleic acids comprising fragments of bases 7-2064 of SEQ ID NO:3 as small as 23 nucleotides, or variants with 95% homology to bases 7-2064 of SEQ ID NO:3 or the fragments, DNA constructs comprising those nucleic acids, plants, plant cells and seeds transformed with those DNA constructs, and a method of using an ADF promoter to express a heterologous nucleic acid in a plant.

The instant specification, however, only provides guidance for the isolation of the MIP synthase cDNA from maize embryo cDNA by PCR with primers based on the yeast gene sequence and the use of the cDNA to probe a maize cDNA library (Example 1), analysis of MIP synthase expression patterns in maize seed (Example 2), cloning of the flanking sequences from maize genomic DNA and their sequencing (Example 3), and operable linkage of the *gus* coding sequence to the full-length version of this isolated MIP synthase promoter (bases 7-2064 of SEQ

ID NO:3) and in transient expression of GUS in maize embryos and stable expression in maize callus and plants (examples 3-7).

The instant specification fails to provide guidance for which nucleotides of bases 7-2064 of SEQ ID NO:3 can be altered and to which other nucleotides, and which nucleotides must not be changed, to maintain promoter and expression enhancing activity, respectively, in the variant DNAs. The specification also fails to provide guidance for which nucleotides can be deleted, or for how to make the deletions, to produce the claimed fragments and still produce a functional promoter or enhancer.

Twenty-three base-pair long regions of a DNA fragment that has promoter activity cannot predictably be assumed to also have promoter activity. Deletion analysis of various promoters have shown that even DNA segments from the portion of a promoter region containing sequence elements thought to be most important (*e.g.*, the TATA-box) need to be longer than 23 basepairs. Maiti et al (1997, Transgen. Res., 6:143-156), in studies on a figwort mosaic virus promoter, found that smallest portion upstream of the transcriptional start site of that would support transcription was 198 basepairs long; segments of 73 and 37 basepairs did not work (Fig. 4).

Mutation of promoter sequences also produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724).

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate a multitude of nucleic acids comprising bases 7-2064 of SEQ ID NO:3 or fragments (including those as small as 23 nucleotides) or variants with 95% homology to those nucleic acids. Making

all possible 23 consecutive nucleotide fragments of bases 7-2064 of SEQ ID NO:3 would require generation and analysis of 2035 fragments. Making all possible single base full-length variants would require making and analyzing 3^{2058} variants; these variants would have 99.9% identity to SEQ ID NO:3. Because nucleic acids with 95% identity to SEQ ID NO:3 would have up to 102 nucleotide substitutions, many more than 19^{2058} nucleic acids would need to be made and analyzed. The unpredictability discussed above suggests that none of the 23 base fragments would even function. Thus, without guidance, undue experimentation would be required to generate and analyze these fragments and variants.

Therefore, the specification is not enabled for a multitude of nucleic acids comprising fragments of bases 7-2064 of SEQ ID NO:3 as small as 23 nucleotides, or variants with 95% homology to bases 7-2064 of SEQ ID NO:3 or the fragments, DNA constructs comprising those nucleic acids, plants, plant cells and seeds transformed with those DNA constructs, and a method of using an ADF promoter to express a heterologous nucleic acid in a plant.

Applicant urges that fragments of bases 7-2064 of SEQ ID NO:3 of 23 nucleotides have utility as a probe capable of hybridizing to MIP promoter sequences and use of portions of promoter sequences as probes is well known in the art in PCR (response pg 3).

This is not found persuasive because the specification does not teach which 23 base fragment (or variant thereof) would be capable of isolating other MIP promoters, nor does it teach the specific hybridization or PCR conditions for isolating homologues. Furthermore, it is noted that use as a probe for isolating homologues is not a specific and substantial utility.

7. Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 6 December 2002, as applied to claims 9-12 and 14-16. Applicant's arguments filed 1 April 2003 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of nucleic acids comprising fragments of bases 7-2064 of SEQ ID NO:3 as small as 23 nucleotides, or variants with 95% homology to bases 7-2064 of SEQ ID NO:3 or the fragments, DNA constructs comprising those nucleic acids, plants, plant cells and seeds transformed with those DNA constructs, and a method of using an ADF promoter to express a heterologous nucleic acid in a plant.

In contrast, the specification only describes a promoter from maize that comprises bases 7-2064 of SEQ ID NO:3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Furthermore, the claims do not include functional language for the claimed nucleic acids.

Hence, Applicant has not, in fact, described nucleic acids comprising fragments of bases 7-2064 of SEQ ID NO:3 as small as 23 nucleotides, or variants with 95% homology to bases 7-2064 of SEQ ID NO:3 or the fragments within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

Applicant urges that claims 17 and 24 include the 3' end of the MIP promoter (response pg 3). This is not found persuasive because Applicant does not recite functional language in the claim and does not describe 200 base long nucleic acids with 95% identity to SEQ ID NO:3 and that have promoter activity.

8. Claims 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 17, line 3, claim23, line 4, and claim 24, line 5, are indefinite in their recitation of "homology". It is not clear what is intended by this term - does "homology" mean that the claimed nucleic acid has 95% identity to the claimed portions of SEQ OD NO:3 or does "homology" mean that only certain nucleotide substitutions are permitted (and if the latter, what are those substitutions)?

Claim 18 is improperly drawn to the nucleic acid molecule of claim 17, when the claim should be drawn to a construct comprising the nucleic acid molecule of claim 17 operably linked to a heterologous nucleic acid sequence. Dependent claims will need to be amended accordingly.

Claim 23, line 3, appears to be missing a word before "7-2064". Is that word --bases--?

9. Claims 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to a method of produced transformed plant tissue capable of expressing a heterologous nucleic acid sequence. However, at no time is a plant cell, a plant tissue or plant transformed with the heterologous nucleic acid. Claim 24 should be amended to state that a construct comprising the nucleic acid sequence, as recited in lines 3-6, operably linked to a heterologous nucleic acid sequence is introduced into at least one plant cell. Additionally, no steps in claim 24 are drawn to the production of plant tissue. Lastly, claim 26 is missing a step in which the progeny are selected for those that also comprise the construct; not all progeny of a transformed plant will contain the construct with which the plant was transformed.

Claim Rejections - 35 USC § 102

10. Claim 23 is rejected under 35 U.S.C. 102(e) as being anticipated by Lappegard et al (US Patent 6,225,529, filed August, 1998).

Lappegard et al teach a 26 base long nucleic acid with 96.1% identity to bases 7-2064 of SEQ ID NO:3 (bases 668-694). Lappegard et al teach a nucleic acid with "at least about" 23 contiguous nucleotides of bases 7-2064 of SEQ ID NO:3 (bases 871-892). This nucleic acid is a MIP synthase promoter (column 3, lines 1-5). Lappegard et al also teach plants and seeds transformed with constructs comprising the nucleic acid and a method of using it to express a heterologous nucleic acid in a plant seed (claims 23-33).

11. Claims 17-22 and 24-26 are free of the prior art, given the failure of the prior art to teach or suggest a nucleic acid of bases 7-2064 of SEQ ID NO:3 or comprising a nucleic acid with 95% homology to bases 1864-2064 of SEQ ID NO:3.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
June 2, 2003